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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 766,873	01 19 2001	Hongsheng Su	104385.132	9057

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HALE AND DORR, LLP
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BOSTON, MA 02109

EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06 03 2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/766,873

Applicant(s)

SU ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 3/12/2003.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 23-25 and 27-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-22, 26 and 30-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Applicants amendment of claims 1, 4, 12 and 14, and the addition of claim 35, Paper No. 9, 3/24/2003, is acknowledged. Applicants' arguments filed on 3/24/2003, Paper No. 9, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1-35 are still at issue and are present for examination.

Claim Objections

Claim 1 is objected to because of the following informalities:

Claim 1 recites "...of a Protein coded by a homologous or heterologous coding sequence...". It is suggested that this be amended to "...of a Protein encoded by a homologous or heterologous coding sequence...".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22, 26 and 30-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

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to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as applied to claims 1-11, 13-21, 26 and 30-34. In response to this rejection applicants have amended the claims and traverse the rejection as it applies to the amended claims.

Applicants traverse the above rejection based on a lack of written description in combination with the rejection based on a lack of enabling disclosure below.

Applicants arguments that appear to be addressed to the written description rejection will be addressed here and those that appear to be address the rejection based on a lack of enabling disclosure will be addressed below.

Applicants assert that the specification includes a sufficient description of a variety of proteins and selectable markers which were successfully expressed in *Flavobacterium heparinum* host cells. In response to this argument, applicant is reminded that applicants claims are drawn to all *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein. The mere description of a variety of proteins and selectable markers which applicants successfully expressed in *Flavobacterium heparinum* does not adequately describe the breadth of the claims as they are now amended to include all *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein. As pointed out by applicants comments, "The description clearly allows persons of ordinary skill in the art to recognize that the inventor invented what is claimed, a new host system for expressing

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recombinant DNA". Applicants invention of a new host system for expressing DNA is recognized, however applicants new host system is not representative of any host system which employs any *Flavobacterium heparinum* host cells transformed with any recombinant DNA constuction effective to cause expression of any protein.

Given the lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-22, 26 and 30-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Flavobacterium heparinum* transformed with pIBFX1 and pIBFX2, does not reasonably provide enablement for a *Flavobacterium heparinum* transformed with any vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as applied to claims 1-11, 13-21, 26 and 30-34. In response to this rejection applicants have amended the claims and traverse the rejection as it applies to the amended claims.

Applicants traverse the above rejection based on a lack of enabling disclosure in combination with the rejection based on a lack of written description above.

Applicants' arguments that appear to be addressed to a lack of enabling disclosure rejection will be addressed here and those that appear to be address the rejection based on a lack written description are addressed above.

Applicants assert that given the disclosure in the specification, one skilled in the art would be able to use various vectors and express different proteins without undue experimentation. It is acknowledged that given applicants' disclosure, one of skill in the art would be able to use the vectors disclosed by applicants, pIBFX1 and pIBFX2 to express different proteins without undue experimentation, however this disclosure combined with the knowledge of one of ordinary skill in the art does not enable the breadth of the claims which read on any *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein. As discussed above under the written description rejection, the mere disclosure of a number of different homologous and heterologous proteins and selectable markers that applicants expressed in *Flavobacterium heparinum* does not enable the breadth of the claims which read on any *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein. Applicants' comments with respect to guidance in the specification regarding other such proteins that may be used by the skilled artisan by routine methods are somewhat unclear and do not support applicants' assertions that applicants have given sufficient guidance as to the necessary features of any *Flavobacterium heparinum* host cell

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expression system. Again applicant is reminded that applicants claims read on any host system which employs any *Flavobacterium heparinum* host cells transformed with any recombinant DNA construction effective to cause expression of any protein. As discussed above and pointed out by applicants comments, "The description clearly allows persons of ordinary skill in the art to recognize that the inventor invented what is claimed, a new host system for expressing recombinant DNA". Applicants invention of a (single) new host system for expressing DNA is recognized, however applicants new host system is not representative of any (all possible) host systems which employs any *Flavobacterium heparinum* host cell transformed with any recombinant DNA construct effective to cause expression of any protein. Regardless of the level of knowledge and skill in the art applicants must give guidance as to the necessary characteristics of any *Flavobacterium heparinum* host cell expression system such as the necessary attributes of the recombinant DNA construct needed to transform a *Flavobacterium heparinum* host cell such as replication origins, or integration sequences in combination with selectable markers etc.... The mere disclosure of a few selectable markers does not enable the claimed genus which encompasses any *Flavobacterium heparinum* host cell transformed with any recombinant DNA construct effective to cause expression of any protein.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any *Flavobacterium heparinum* transformed with any vector. The scope of the claims must bear a reasonable

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correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 13-21, 26 and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al. (WO 96/01894, January 25, 1996) and McBride et al. (Applied and Environmental Microbiology, Vol. 62, No. 8, pages 3017-3022, August 1996).

The rejection is stated in the previous office action as applied to claims 1-11, 13-21, 26 and 30-34. In response to this rejection applicants have amended the claims and traverse the rejection as it applies to the amended claims.

Applicants traverse the rejection based on the following: Applicants submit that the reference Zimmerman et al. contains one sentence which states that the cloned genes encoding chondroitinase AC and chondroitinase B can be used in conjunction with suitable expression systems to produce the enzymes in *Flavobacterium*, for

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example under control of overexpression promoters. Applicants are reminded that only a single sentence, as pointed out by applicants, is necessary to provide a suggestion to produce the claimed *Flavobacterium* expression system. Clearly Zimmerman provides this suggestion and thus the motivation to produce the claimed *Flavobacterium heparinum* host cell expression system. Applicants further point out that Zimmerman in the remainder of their discussion, discuss how *Flavobacterium heparinum* gene libraries were created in *E. coli* with no mention of any attempted or successful expression in *Flavobacterium heparinum*. Applicants is again reminded that this is a 103 rejection based on obviousness and Zimmerman is depended on to provide the motivation and suggestion that one of ordinary skill in the art would want to produce the claimed *Flavobacterium heparinum* expression system.

Applicants further traverse that based on the above discussed one sentence in Zimmerman et al., one of skill in the art would not have had a reasonable expectation of success in using this host system. As previously stated, the reasonable expectation of success comes from the results of McBride et al. who successfully used the Tn4351 transposon to introduce heterologous DNA into *Flavobacterium meningosepticum*. In addition McBride et al. teach that the same Tn4351 transposon was successfully introduced by conjugation into *Cytophaga hutchinsonii*, *Cytophaga hutchinsonii*, *Flexibacter Canadensis*, *Flexibacter* sp. strain FS1 and *Sporocytophaga myxocoides*, further adding to the expectation of successfully using the Tn4351 transposon to genetically manipulate *Flavobacterium heparinum*.

With respect to applicants traversal as it applies to McBride et al., applicants submit that McBride et al. does not teach the transformation of *Flavobacterium heparinum* with a DNA construct effective to cause expression of a protein coded by a homologous or heterologous coding sequence placed under control of a regulatory region effective in *Flavobacterium heparinum*, as claimed by applicants amended claims. In response applicants is again reminded that this is a 103 rejection based on obviousness as a result of the combination of the two references, Zimmerman et al. and McBride et al., and as discussed above McBride et al. did successfully introduce the transposon Tn4351 by conjugation into *Cytophaga hutchinsonii*, *Cytophaga hutchinsonii*, *Flexibacter Canadensis*, *Flexibacter* sp. strain FS1 and *Sporocytophaga myxocoides*, wherein said transposon integrated into the host chromosomes and conferred erythromycin resistance thus the integrated transposon Tn4351 lead to the expression of a heterologous protein in each of the above discussed bacterial species.

Newly added claim 35 is also included in this rejection on the basis that the limitation which it adds, wherein said recombinant DNA encodes for a polypeptide or protein selected from the group consisting of heparinase I, heparinase II, heparinase III and selectable markers" is also obvious as any recombinant DNA used to express the genes encoding the *Flavobacterium heparinum* enzymes, chondroitinase AC and chondroitinase B, in *Flavobacterium heparinum* would have also included a selectable marker that would be used to assert pressure that the recombinant DNA construct be maintained in the presence of the corresponding antibiotic etc... Such a selectable

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marker was included in the Tn4351 transposon used by McBride et al. as discussed above, that of erythromycin resistance.

Thus claims 1-11, 13-21, 26 and 30-35 are obvious by Zimmerman et al. and McBride et al.

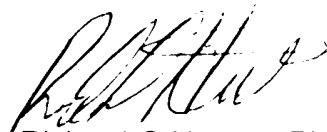
Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgH
June 2, 2003